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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,454	11/29/2005	Ichiro Hirao	0230-0222PUS1	8799

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
07/11/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/521,454	HIRAO ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4-02-08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *2-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2-15 are presently pending for examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendments/Arguments

Claim Objections

3. The objection to claims 4-10 set forth in the prior Office Action is withdrawn in response to Applicant's amendment of these claims.

Claim Rejections - 35 USC § 102

4. The rejection of claim 1 is withdrawn in response to Applicant's amendment cancelling this claim.

Claim Rejections - 35 USC § 103

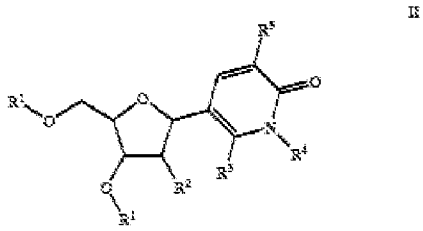
5. The rejection of claim 1 under 35 USC 103(a) is withdrawn in response to Applicant's cancellation of this claim.

6. Applicant's arguments with respect to claims 1-3 have been considered but are moot in view of the new ground(s) of rejection.

7. Claims 2-9, and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Froehler et al. (US Patent NO. 6447998 or 6495672 or US application number 20030120065), in view of Ohtsuki et al. and Guo et al. (1998; Applicant's IDS filed)

8. Froehler et al. discloses 2-aminopyridine and 2-pyridone C-nucleosides and oligonucleotides containing the subject nucleosides. The nucleosides are useful in the

preparation of the subject oligonucleotides. The oligonucleotides are useful in oligonucleotide-based diagnosis and separation through triplex binding. In one embodiment these modified nucleobases comprise the following structure (see col. 2):



II

wherein:

each R^1 is independently H or a hydroxy protecting group, or both R^1 groups are taken together to form a cyclic hydroxy protecting group;

R^2 is H, F, $—OR^1$, or $—OR^2$;

R^3 is H or $—CH_3$;

each R^4 of formula I and II is independently H or an amine protecting group, or both R^4 groups of formula I are taken together to form a cyclic amine protecting group;

R^5 is H, $—CH_3$, or $—C{\equiv}C—CH_3$; and

9. However, the nucleosides or nucleotides of Froehler et al. comprise a structure that differs from the instant claims to the extent that the positions at which the ribose and the substituents groups are attached to the pyridine ring are different.

10. Guo et al. teach that pyrimidine nucleotide analogues lacking the 2-keto group inhibit DNA polymerase reactions.

Ohtsuki et al. discloses the following unnatural nucleobase (see m^5y base):

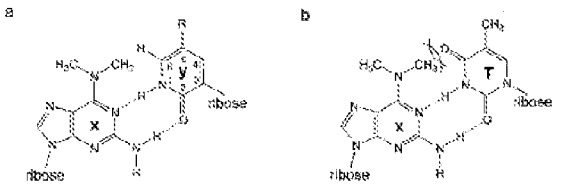


Fig. 1. The unnatural x-y (y: R = H, m^5y: R = CH_3) pair (a) in comparison with a noncognate x-T pair (b).

It would have been obvious to the ordinary skilled art seeking alternative nucleobases to vary the positions of the substituents in the pyridine ring to produce another nucleobase to be used for the same purpose, namely for incorporation into nucleic acid molecules. One of ordinary skill in the art would have been motivated to modify the teachings of Froehler et al. to design the molecules of the instant invention, by modifying the pyrimidine analogue to comprise a 2-keto group since it was known in the prior art at the time of filing that such groups are necessary for interaction with DNA polymerase. One of ordinary skill in the art would have had a reasonable expectation of success in making this modification since the prior art teaches the ordinary skilled artisan how to make pyrimidine nucleosides analogues comprising a 5-substituent (see Froehler et al.) and a 2-keto group (Ohtsuki et al.), and further teaches how to incorporate these analogues into nucleic acid (see Ohtsuki et al.)

Moreover, with respect to claims 4 and 12 that are limited to wherein the 5-position of the base is substituted with an iodine or biotin derivative, it is noted that the cited prior art describes nucleoside structures comprising 5-substitutions including wherein the substituents is hydrogen, methyl, and alkynyl groups. The instantly claimed compounds, are considered to be obvious analogues of the prior art compounds due to the close structural similarity to the prior art compounds, and to the extent that there does not appear to be a critical role for the substituents of the 5'-position. See MPEP § 2144.09 which states:

> **2144.09 Close Structural Similarity Between Chemical Compounds (Homologs, Analogues, Isomers)**

REJECTION BASED ON CLOSE STRUCTURAL SIMILARITY IS FOUNDED ON THE EXPECTATION THAT COMPOUNDS SIMILAR IN STRUCTURE WILL HAVE SIMILAR PROPERTIES

A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (discussed in more detail below) and *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991) (discussed below and in MPEP § 2144) for an extensive review of the case law pertaining to obviousness based on close structural similarity of chemical compounds. See also MPEP § 2144.08, paragraph II.A.4.(c).

HOMOLOGY AND ISOMERISM ARE FACTS WHICH MUST BE CONSIDERED WITH ALL OTHER RELEVANT FACTS IN DETERMINING OBVIOUSNESS

Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977). See also In re May, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (stereoisomers prima facie obvious).

Therefore, the invention as a whole would have been prima facie obvious over the teachings of Froehler et al. in view of Guo et al. and Ohtsuki et al.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 2-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (New Matter).

Claim 2 and those claims dependent therefrom recite "biotin, dichloroacetyl group, fluorescein, 6-carboxyfluorescein, tetramethyl-6-carboxyrhodamine, or derivatives thereof introduced via a linker selected from an aminoalkyl group, an aminoalkenyl group and an aminoalkynyl group."

The specification as filed recites the following at paragraph [0067]: "[T]o introduce biotin as a substituent at the 5-position of the nucleoside or nucleotide of the present invention, biotin may be introduced directly, but preferably via a linker selected from an aminoalkyl group, an aminoalkenyl group and an aminoalkynyl group. For example, in Examples 11-15 of the present invention (FIGS. 15-18), biotin was introduced at the 5-position of y via either of two linkers, ethylenic or acetylenic. As used herein, the term "biotin derivative" is intended to also include biotin modified to have a linker for introduction into nucleosides or nucleotides."

It is noted that there is no support in the specification as filed for derivatives of dichloroacetyl group, fluorescein, 6-carboxyfluorescein, tetramethyl-6 carboxyrhodamine introduced at the 5- position of the nucleotide or nucleoside of the invention via a linker selected from an "aminoalkyl group, an aminoalkenyl group and an aminoalkynyl group."

Applicant's amendment is therefore considered to add new matter to the scope of the claimed invention, since the full scope of the claimed invention does not find support in the specification as originally filed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner, Art Unit 1633

JLE